In the Claims

Please amend the claims as follows:

5. (amended) The amphiphilic drug-oligomer conjugate of claim 1 wherein the therapeutic compound is a peptide or protein [and the peptide is] selected from the group consisting of: enkephalin, adrenocorticotropic hormone, adenosine deaminase ribonuclease, alkaline phosphatase, angiotensin, antibodies, arginase, arginine deaminease, asparaginase, caerulein, calcitonin, chemotrypsin, cholecystokinin, clotting factors, dynorphins, endorphins, endorphins, enkephalins, enkephalins, erythropoietin, gastrin-releasing peptide, glucagon, hemoglobin, hypothalmic releasing factors, interferon, katacalcin, motilin, neuropeptide Y, neurotensin, non-naturally occurring opioids, oxytosin, papain, parathyroid hormone, peptides prolactin, soluble CD-4, somatomedin, somatostatin, somatostatin, somatotropin, superoxide dismutase, thyroid stimulating hormone, tissue plasminogen activator, trypsin, vasopressin and analogues and active fragments thereof.

6. (amended) The amphiphilic drug-oligomer conjugate of claim 1 wherein the therapeutic compound is an [Opioid] opioid receptor agonist, antagonist or partial agonist/partial antagonist.

10. (amended) The [The] amphiphilic drug-oligomer conjugate of claim 1 wherein the lipophilic moiety is coupled to the hydrophilic moiety by a bond selected from the group consisting of: amide bond, carbamate bond, carbonate bond and ester bond.

11. (amended) The amphiphilic drug-oligomer conjugate of claim 1 wherein the oligomer moiety is coupled to the drug moiety by a bond selected from the group consisting of amide bond, carbamate bond, carbonate bond, and ester bond.

13. (amended) The amphiphilic drug-oligomer conjugate of claim 1 wherein the hydrophilic moiety is selected from the group consisting of sugars [or] and PEG_{1-7}.

14. (amended) The amphiphilic drug-oligomer conjugate of claim 1 wherein the hydrophilic moiety comprises a sugar and the sugar is selected from the group consisting of: amino sugars [and non-amino sugars].

15. (amended) The amphiphilic drug-oligomer conjugate of claim 1 wherein the oligomer is selected from the group consisting of:

$CH_3(CH_2)_n(OC_2H_4)_mOH$ (Formula 1)$_s$[;]

wherein n=3 to 25 and m=1 to 6;

$CH_3(CH_2)_n(OC_2H_4)_mOCH_2CO_2H$ (Formula 2)$_s$[;]

wherein n=3 to 25 and m=1 to 7;

$CH_3(CH_2)_nCX(OC_2H_4)_mOH$ (Formula 3)$_s$[;]

wherein n=3 to 25, m=1 to 7 and X=O or N;

$R\text{-}(OC_2H_4)_mCH_2CO_2H$ (Formula 4)$_s$

wherein m=0 to 5 and R=cholesterol or adamantane; [or]

$R\text{-}OCO(C_2H_4O)_mCH_2CO_2H$ (Formula 5)[;]$_s$

wherein m=0 to 5;

$CH_3(CH_2\text{—}CH\overline{]}CH)_6(CH_2)_2CH_2(OC_2H_4)_mOH$ (Formula 6)[;]$_s$

wherein m=0 to 7; and

$CH_3(CH_2—CH]CH)_6(CH_2)_2C_X(OC_2H_4)_mOH$ (Formula 7)[;],

wherein m=1 to 7 and X=N or O.

16. (amended) The [method] amphiphilic drug-oligomer conjugate of claim 1 wherein the hydrophilic moiety comprises a sugar and the sugar is selected from the group consisting of [amino sugars and] non-amino sugars.

17. (amended) The [method] amphiphilic drug-oligomer conjugate of claim 1 wherein the hydrophilic moiety comprises a monosaccharide.

18. (amended) [An] The amphiphilic drug-oligomer conjugate of claim 1 wherein the oligomer is selected from the group consisting of:

$CH_3(CH_2CH=CH)_6(CH_2)_2CH_2(OC_2H_4)_mOH$,

where m=1 to 7;

$CH_3(CH_2CH=CH)_6(CH_2)_2CO(OC_2H_4)_mOH$,

where m=1 to 7;

$CH_3(CH_2CH=CH)_6(CH_2)_2CONHCH_2CH_2(OC_2H_4)_mOH$,

where m=1 to 6;

$CH_3(CH_2CH=CH)_6(CH_2)_3(OC_2H_4)_mOCH_2COOH$,

where m=1 to 6;

$CH_3(CH_2CH=CH)_6(CH_2)_2CO(OC_2H4)_mOCH_2COOH$,

where m=1 to 6;

$CH_3(CH_2)_7CH=CH(CH_2)_8(OC_2H_4)_mOH$,

where m=1 to 7;

$CH_3(CH_2)_7CH=CH)(CH_2)_7CO(OC_2H_4)_mOH$,

where m=1 to 7;

$CH_3(CH_2)_7CH=CH(CH_2)_7CONHCH_2CH_2(OC_2H_4)_mOH$,

where m=1 to 6;

$CH_3(CH_2)_7CH=CH(CH_2)_8(OC_2H_4)_mOCH_2COOH$,

where m=1 to 6;

$CH_3(CH_2)_7CH=CH(CH_2)_7CO(OC_2H_4)_mOCH_2CH_2OH$,

where m=1 to 6;

$CH_3(CH_2)_4CH=CHCH_2CH=CH(CH_2)_7CH_2(OC_2H_4)_mOH$,

where m=1 to 6;

$CH_3(CH_2)_4CH=CHCH_2CH=CH(CH_2)_7CO(OC_2H_4)_mOH$,

where m=1 to 7;

$CH_3(CH_2)_4CH=CHCH_2CH=CH(CH_2)_7CONHCH_2CH_2(OC_2H_4)_mOH$,

where m=1 to 6;

$CH_3(CH_2)_4CH=CHCH_2CH=CH(CH_2)_7CO(OC_2H_4)_mOCH_2COOH$,

where m=1 to 6;

$CH_3(CH_2)_4CH=CHCH_2CH=CH(CH_2)_7CH_2(OC_2H_4)_mOCH_2COOH$,

where m=1 to 6;

$CH_3(CH_2CH=CH)_3(CH_2)_7CH_2(OC_2H_4)_mOH$,

where m=1 to 7;

$CH_3(CH_2CH=CH)_3(CH_2)_7CO(OC_2H_4)_mOH$,

where m=1 to 7;

$CH_3(CH_2CH=CH)_3(CH_2)_7CONHCH_2CH_2(OC_2H_4)_mOH$,

where m=1 to 6;

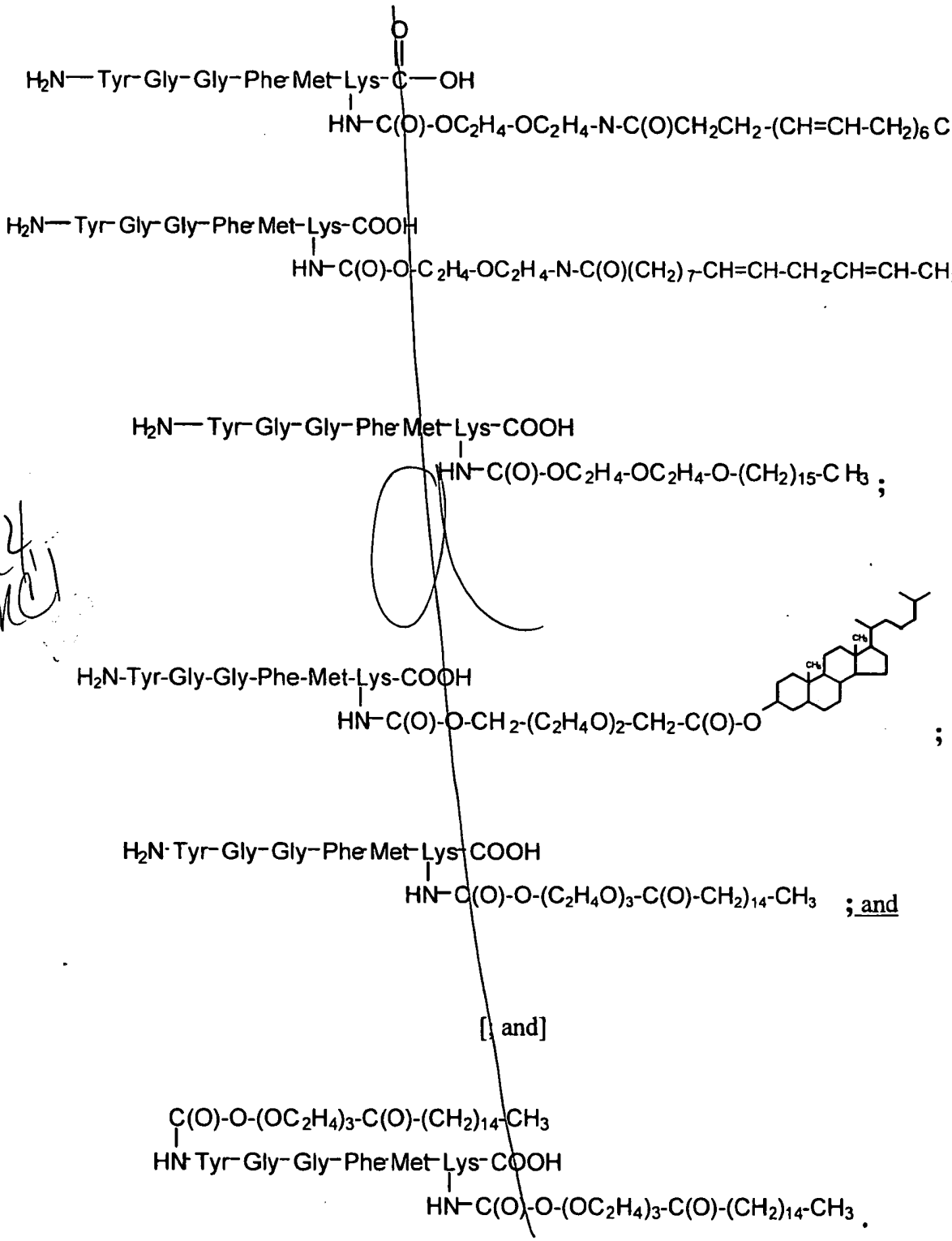
$CH_3(CH_2CH=CH_3(CH_2)_7CO(OC_2H_4)_mOCH_2COOH$,

where m=1 to 6; and

$CH_3(CH_2CH=CH_3(CH_2)_7CH_2(OC_2H_4)_mOCH_2COOH$,

where m=1 to 6.

20. (amended) An amphiphilic oligomer-enkephalin conjugate selected from the group consisting of:


H2N—Tyr-Gly-Gly-Phe-Met-Lys-C—OH
HN-C(O)-OC2H4-OC2H4-N-C(O)CH2CH2-(CH=CH-CH2)6 CH3 ;
H2N—Tyr-Gly-Gly-Phe-Met-Lys-COOH
HN-C(O)-O-C2H4-OC2H4-N-C(O)(CH2)7-CH=CH-CH2CH=CH-CH2-CH3;
H2N—Tyr-Gly-Gly-Phe-Met-Lys-COOH
HN-C(O)-OC2H4-OC2H4-O-(CH2)15-CH3 ;
H2N-Tyr-Gly-Gly-Phe-Met-Lys-COOH
HN-C(O)-O-CH2-(C2H4O)2-CH2-C(O)-O
;
H2N-Tyr-Gly-Gly-Phe-Met-Lys-COOH
HN-C(O)-O-(C2H4O)3-C(O)-CH2)14-CH3 ; and
[; and]
C(O)-O-(OC2H4)3-C(O)-(CH2)14-CH3
HN-Tyr-Gly-Gly-Phe-Met-Lys-COOH
HN-C(O)-O-(OC2H4)3-C(O)-(CH2)14-CH3 .

24. (amended) The method of claim [18] 23 further characterized in that said conjugate exhibits activity in the without cleavage of the therapeutic compound from the oligomer.

25. (amended) The method of claim [18] 23 wherein the receptor is a G-protein coupled receptor.

26. (amended) The method of claim [18] 23 wherein the receptor is an [Opioid] opioid receptor.

27. (amended) The method of claim [18] 23 wherein the receptor is a [Opioid] opioid receptor; selected from the group consisting of δ, μ, and κ receptors.

28. (amended) The method of claim [18] 23 wherein the hydrophilic moiety is selected from the group consisting of sugar and PEG_{1-7}.

29. (amended) The method of claim [18] 23 wherein the hydrophilic moiety is selected from the group consisting of fatty acid, alkyl 1-26, cholesterol and adamantane.

30. (amended) The method of claim [18] 23 wherein the therapeutic compound is a peptide having an added N-terminal residue selected from the group consisting of proline[,] and alanine.

31. (amended) The method of claim [18] 23 wherein the therapeutic compound is a peptide or protein.

32. (amended) The method of claim [18] 23 wherein the therapeutic compound is a peptide [and the peptide is] or protein selected from the group consisting of: enkephalin, adrenocorticotropic hormone, adenosine deaminase ribonuclease, alkaline phosphatase, angiotensin, antibodies, arginase, arginine deaminease, asparaginase, caerulein, calcitonin, chemotrypsin, cholecystokinin, clotting factors, dynorphins, endorphins,

endorphins, enkephalins, enkephalins, erythropoietin, gastrin-releasing peptide, glucagon, hemoglobin, hypothalmic releasing factors, interferon, katacalcin, motilin, neuropeptide Y, neurotensin, non-naturally occurring opioids, oxytosin, papain, parathyroid hormone, peptides prolactin, soluble CD-4, somatomedin, somatostatin, somatostatin, somatotropin, superoxide dismutase, thyroid stimulating hormone, tissue plasminogen activator, trypsin, vasopressin, and analogues and active fragments of such peptides.

33. (amended) The method of claim [18] 23 wherein the amphiphilic oligomer is selected from the group consisting of:

$CH_3(CH_2)_n(OC_2H_4)_mOH$ (Formula 1)[;],

wherein n=3 to 25 and m=1 to 6;

$CH_3(CH_2)_n(OC_2H_4)_mOCH_2CO_2H$ (Formula 2)[;],

wherein n=3 to 25 and m=1 to 7;

$CH_3(CH_2)_nCX(OC_2H_4)_mOH$ (Formula 3)[;],

wherein n=3 to 25 , m=1 to 7 and X=O or N;

$R\text{-}(OC_2H_4)_mCH_2CO_2H$ (Formula 4),

wherein m=0 to 5 and R=cholesterol or adamantane; or

$R\text{-}OCO(C_2H_4O)_mCH_2CO_2H$ (Formula 5)[;],

wherein m=0 to 5;

$CH_3(CH_2—CH\overline{]}CH)_6(CH_2)_2CH_2(OC_2H_4)_mOH$ (Formula 6)[;],

wherein m=0 to 7; and

$CH_3(CH_2—CH=CH)_6(CH_2)_2C_X(OC_2H_4)_mOH$ (Formula 7)[;],

wherein m=1 to 7 and X=N or O.

34. (amended) The method of claim [18] 23 wherein the hydrophilic moiety is coupled to the hydrophobic moiety by a hydrolyzable bond.

35. (amended) The method of claim [18] 23 wherein the hydrophilic moiety is coupled to the hydrophobic moiety by a non-hydrolyzable bond

37. (amended) The method of claim [31] 36 wherein the therapeutic compound is a peptide or protein.

38. (amended) The method of claim [31] 36 wherein the therapeutic compound is a peptide [and the peptide is] or protein selected from the group consisting of: enkephalin, adrenocorticotropic hormone, adenosine deaminase ribonuclease, alkaline phosphatase, angiotensin, antibodies, arginase, arginine deaminease, asparaginase, caerulein, calcitonin, chemotrypsin, cholecystokinin, clotting factors, dynorphins, endorphins, endorphins, enkephalins, enkephalins, erythropoietin, gastrin-releasing peptide, glucagon, hemoglobin, hypothalmic releasing factors, interferon, katacalcin, motilin, neuropeptide Y, neurotensin, non-naturally occurring opioids, oxytosin, papain, parathyroid hormone, peptides prolactin, soluble CD-4, somatomedin, somatostatin, somatostatin, somatotropin, superoxide dismutase, thyroid stimulating hormone, tissue plasminogen activator, trypsin, vasopressin, and analogues and active fragments of such peptides.

39. (amended) The method of claim [31] 36 wherein the therapeutic compound is [met^5] enkephalin.

40. (amended) The method of claim [31] 36 wherein the lipophilic moiety is coupled to the hydrophilic moiety by a hydrolyzable bond.

41. (amended) The method of claim [31] 36 wherein the lipophilic moiety is coupled to the hydrophilic moiety by a non-hydrolyzable bond.

42. (amended) The method of claim [31] 36 wherein the lipophilic moiety is coupled to the hydrophilic moiety by a bond selected from the group consisting of: amide bond, carbamate bond, carbonate bond and ester bond.

43. (amended) The method of claim [31] 36 wherein the oligomer moiety is coupled to the drug moiety by a bond selected from the group consisting of amide bond, carbonate bond, carbamate bond, and ester bond.

44. (amended) The method of claim [31] 36 wherein the lipophilic moiety is selected from the group consisting of fatty acids, C_{1-26}alkyls, and colesterol.

45. (amended) The method of claim [31] 36 wherein the hydrophilic moiety is selected from the group [cobsisting] consisting of sugars, and PEG_{1-7}.

47. (amended) The method of claim [41] 46 wherein the therapeutic compound is [met^5]enkephalin.

48. (amended) The method of claim [41] 46 wherein the lipophilic moiety is selected from the group consisting of fatty acids, C_{1-26} alkyls, and cholesterol.

49. (amended) The method of claim [41] 46 wherein the one or more hydrophilic moieties are selected from the group consisting of sugars and PEG.

50. (amended) The method of claim [41] 46 wherein the hydrophilic moiety comprises a sugar and the sugar is selected from the group consisting of amino sugars and non-amino sugars.

51. (amended) The method of claim [41] 46 wherein the oligomer is selected from the group consisting of:

$CH_3(CH_2)_n(OC_2H_4)_mOH$ (Formula 1)[;],

wherein n=3 to 25 and m=1 to 6;

$CH_3(CH_2)_n(OC_2H_4)_mOCH_2CO_2H$ (Formula 2)[;],

wherein n=3 to 25 and m=1 to 7;

$CH_3(CH_2)_nCX(OC_2H_4)_mOH$ (Formula 3)[;],

wherein n=3 to 25, m=1 to 7 and X=O or N;

$R\text{-}(OC_2H_4)_mCH_2CO_2H$ (Formula 4),

wherein m=0 to 5 and R=cholesterol or adamantane; or

$R\text{-}OCO(C_2H_4O)_mCH_2CO_2H$ (Formula 5)[;],

wherein m=0 to 4 and R=cholesterol or adamantane;

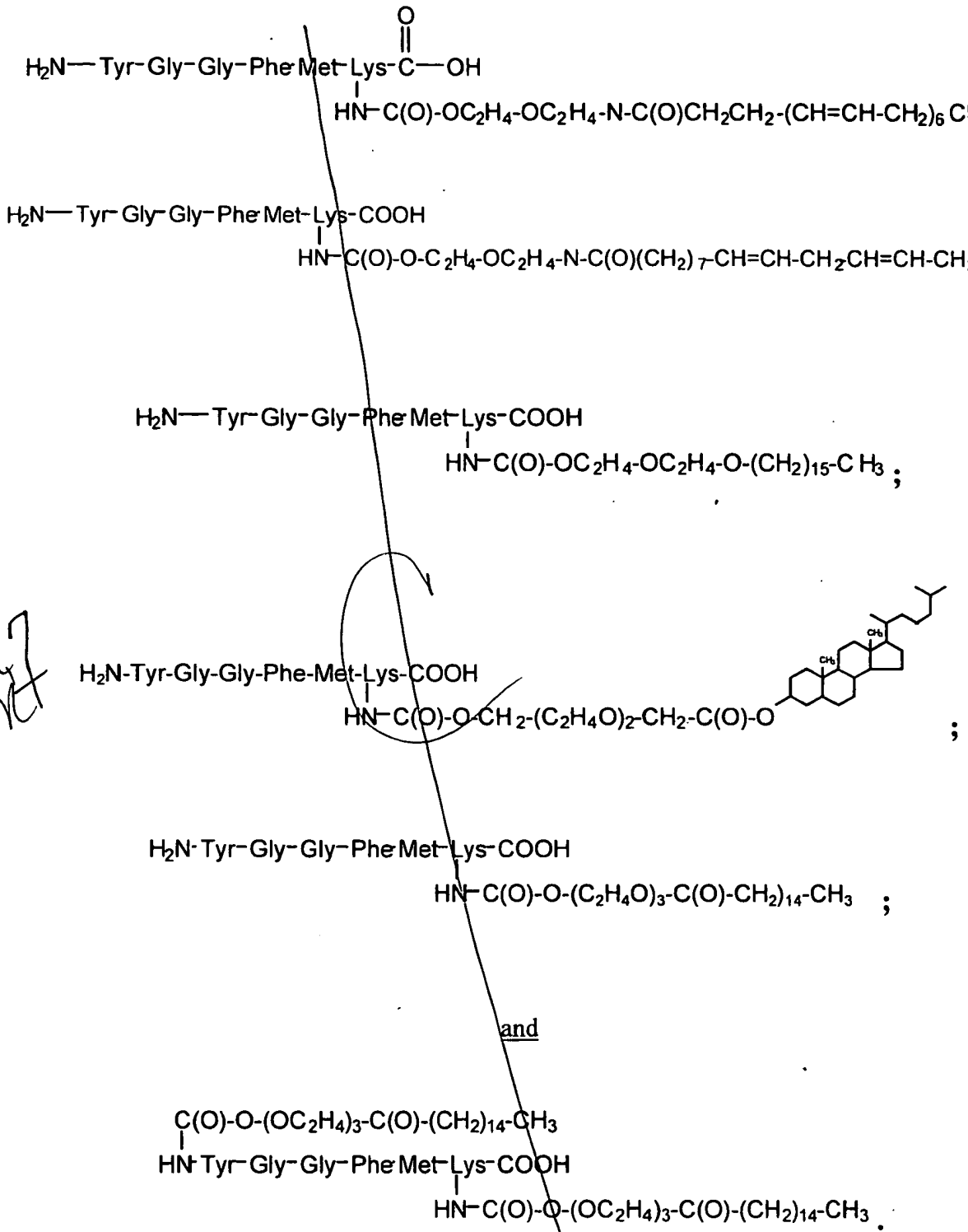
$CH_3(CH_2—CH=CH)_6(CH_2)_2CH_2(OC_2H_4)_mOH$ (Formula 6)[;],

wherein m=0 to 7; and

$CH_3(CH_2—CH=CH)_6(CH_2)_2C_X(OC_2H_4)_mOH$ (Formula 7)[;],

wherein m=1 to 7 and X=N or O.

52. (amended) The method of claim 46 wherein the [An] amphiphilic oligomer-enkephalin conjugate is selected from the group consisting of:



53. (amended) A method for altering the binding affinity of a peptide <u>or protein</u> to its receptor comprising conjugating the peptide to an amphiphilic oligomer comprising a lipophilic moiety coupled to a hydrophilic moiety.

54. (amended) The method according to claim 53 [48 further characterized in that] wherein the binding affinity is increased.

55. (amended) The method according to claim [48 further characterized in that] 53 wherein the binding affinity is reduced.

56. (amended) The method of claim [48] 53 wherein the [peptide is a] peptide or protein is an enkephalin.

57. (amended) The method of claim [48] 56 wherein the peptide or protein is selected from the group consisting of: enkephalin, adrenocorticotropic hormone, adenosine deaminase ribonuclease, alkaline phosphatase, angiotensin, antibodies, arginase, arginine deaminease, asparaginase, caerulein, calcitonin, chemotrypsin, cholecystokinin, clotting factors, dynorphins, endorphins, endorphins, enkephalins, enkephalins, erythropoietin, gastrin-releasing peptide, glucagon, hemoglobin, hypothalmic releasing factors, interferon, katacalcin, motilin, neuropeptide Y, neurotensin, non-naturally occurring opioids, oxytosin, papain, parathyroid hormone, peptides prolactin, soluble CD-4, somatomedin, somatostatin, somatostatin, somatotropin, superoxide dismutase, thyroid stimulating hormone, tissue plasminogen activator, trypsin, vasopressin, and analogues and fragments of such peptides.

58. (amended) The method of claim [48] 56 wherein the [peptides] peptide is [met^5]enkephalin.

59. (amended) The method of claim [48] 53 wherein the lipophilic moiety is selected from the group consisting of fatty acids, C_{1-26}alkyls, and colesterol.

60. (amended) The method of claim [48] 53 wherein the hydrophilic moiety is selected from the group consisting of sugars or PEG_{1-7}.

61. (amended) The method of claim [48] 53 wherein the oligomer is selected from the group consisting of:

$CH_3(CH_2)_n(OC_2H_4)_mOH$ (Formula 1),

wherein n=3 to 25 and m=1 to 6;

$CH_3(CH_2)_n(OC_2H_4)_mOCH_2CO_2H$ (Formula 2),

wherein n=3 to 25 and m=1 to 7;

$CH_3(CH_2)_nCX(OC_2H_4)_mOH$ (Formula 3),

wherein n=3 to 25 , m=1 to 7 and X=O or N;

$R\text{-}(OC_2H_4)_mCH_2CO_2H$ (Formula 4),

wherein m=0 to 5 and R=cholesterol or adamantane; or

$R\text{-}OCO(C_2H_4O)_mCH_2CO_2H$ (Formula 5),

wherein m=0 to 5;

$CH_3(CH_2—CH=CH)_6(CH_2)_2CH_2(OC_2H_4)_mOH$ (Formula 6),

wherein m=0 to 7; and

$CH_3(CH_2—CH=CH)_6(CH_2)_2C_X(OC_2H_4)_mOH$ (Formula 7),

wherein m=1 to 7 and X=N or O.

62. (amended) The amphiphilic drug-oligomer conjugate of claim 1 wherein the therapeutic compound is a peptide [and the peptide is] selected from the group consisting of:

Ac-Phe-Arg-Trp-Trp-Tyr-Lys—NH_2 ;

Ac-Arg-Trp-Ile-Gly-Trp- Lys —NH_2 ;

Trp-Trp-Pro-Lys-His-Xaa—NH_2 ,

wherein Xaa is a naturally-occurring amino acid;

Trp-Trp-Pro-Xaa—NH_2 ,

wherein Xaa is Lys or Arg;

Tyr-Pro-Phe-Gly-Phe-Xaa—NH_2 ,

wherein Xaa is a naturally-occurring amino acid;

(D)Ile-(D)Met-(D)Ser-(D)Trp-(D)Trp-Gly_n-Xaa—NH_2 ,

wherein n is 0 or 1 and wherein Xaa is Gly or the D-form-of a naturally-occurring amino acid;

(D)Ile-(D)Met-(D)Thr-(D)Trp-Gly-Xaa—NH_2 ,

wherein Xaa is Gly or the D-form of a naturally-occurring amino acid;

Tyr-A1-B2-C3—NH_2 ,

wherein A1 is (D)Nve or (D)Nle,

B2 is Gly, Phe, or Trp, and

C3 is Trp or Nap;

Pm and red {Me_xH_y-Tyr-$(NMe)_z$-Tyr-Xaa_z—NH_2},

x is 0, 1, or 2,

y is 0, 1, or 2, and

z is 0 or 1, and

wherein Xaa is Phe, (D)Phe, or NHBzl, with the proviso that x and y together is never greater than 2; and

Trp-Trp-Pro-D4-His_z-Xaa_z—NH_2;

wherein z is 0 or 1,

wherein D4 is Lys or Arg, and

wherein Xaa is a naturally-occurring amino acid.

63. (amended) The method of claim 18 wherein the therapeutic compound is a peptide [and the peptide is] selected from the group consisting of:

Ac-Phe-Arg-Trp-Trp-Tyr-Lys—NH_2;

Ac-Arg-Trp-Ile-Gly-Trp- Lys —NH_2;

Trp-Trp-Pro-Lys-His-Xaa—NH_2,

wherein Xaa is a naturally-occurring amino acid;

Trp-Trp-Pro-Xaa—NH_2,

wherein Xaa is Lys or Arg;

Tyr-Pro-Phe-Gly-Phe-Xaa—NH_2,

wherein Xaa is a naturally-occurring amino acid;

(D)Ile-(D)Met-(D)Ser-(D)Trp-(D)Trp-Gly_n-Xaa—NH_2,

wherein n is 0 or 1 and wherein Xaa is Gly or the D-form-of a naturally-occurring amino acid;

(D)Ile-(D)Met-(D)Thr-(D)Trp-Gly-Xaa—NH_2,

wherein Xaa is Gly or the D-form of a naturally-occurring amino acid;

Tyr-A1-B2-C3—NH_2,

wherein A1 is (D)Nve or (D)Nle,

B2 is Gly, Phe, or Trp, and

C3 is Trp or Nap;

Pm and red {Me_xH_y-Tyr-$(NMe)_z$-Tyr-Xaa_z—NH_2},

x is 0, 1, or 2,

y is 0, 1, or 2, and

z is 0 or 1, and

wherein Xaa is Phe, (D)Phe, or NHBzl, with the proviso that x and y together is never greater than 2;

Trp-Trp-Pro-D4-His_z-Xaa_z—NH_2,

wherein z is 0 or 1,

wherein D4 is Lys or Arg, and

wherein Xaa is a naturally-occurring amino acid.

Please add the following new claims 64 to 72:

64. The amphiphilic drug-oligomer conjugate of claim 1, wherein the therapeutic compound is an opioid.

65. The amphiphilic drug-oligomer conjugate of claim 1, wherein in the therapeutic compound is an enkephalin.

66. The method of claim 23 wherein the therapeutic compound is an opioid receptor agonist, antagonist or partial agonist/partial antagonist.

67. The method of claim 23 wherein the therapeutic compound is an enkephalin.

68. The method of claim 36 wherein the therapeutic compound is an opioid receptor agonist, antagonist or partial agonist/partial antagonist.

69. The method of claim 36 wherein the therapeutic compound is an enkephalin.

70. The method of claim 46 wherein the therapeutic compound is an opioid.